REMARKS

This document is submitted in response to the Office Action dated July 28, 2006 ("Office Action"). Claims 6-17, 20, 22-33 are currently pending. Among them, claims 22-25 have been allowed and claims 16, 17, and 20 withdrawn.

Applicants have amended claims 6 and 7 to promote clarity. Support for "cDNA" recited in amended claim 6 can be found at page 17, lines 1-6, in the specification. No new matter has been introduced. Upon entry of the amendments, claims 6-15 and 26-33 will be under examination.

Reconsideration of the claims, as amended, is respectfully requested in view of the following remarks.

Claim Objection

Applicants have amended claim 6 following the Examiner's instructions and respectfully request withdrawal of this objection.

Rejections under 35 USC § 102

The Examiner rejects claims 6-9 and 30-33 as being anticipated by Lin et al. ("Lin"). More specifically, the Examiner alleges that Lin discloses

> a DNA which comprises the nucleotide sequence (positions 54079-55912) of a BAC clone having 100% sequence identity with SEQ ID NO:20 of instant application. The nucleotide sequence from position 54079-55912 of reference encompass instant SEQ ID NO:20, encoding instant SEQ ID NO:9, which is also a part of an expression vector BAC clone.

Applicants respectfully disagree. It is well established that the novelty requirement would be satisfied when the subject matter of an invention is merely different from what is known in the art. In this case, independent claim 1, as amended, covers an isolated nucleic acid including a **cDNA** sequence that encodes a polypeptide whose amino acid sequence is at least 70% identical to SEQ ID NO:9.

Lin teaches a BAC clone containing the **genomic** sequence of Arabidopsis thaliana chromosome III. It also predicts possible genes located in this genomic sequence, one of which (position 54079 to 55912) encodes a polypeptide having an identical amino acid sequence to SEQ ID NO:9. This predicted gene contains five exons separated by **four introns**. See page 9. The nucleotide sequence of this gene, **when excluding the intron sequences**, matches SEQ ID NO:20, which encodes SEQ ID NO:9.

As well known in the art, a cDNA sequence is a continuous coding region while a genomic sequence, in most cases, contains fragmented coding regions interrupted by intron sequences. The claimed nucleic acid, e.g., SEQ ID NO:20, clearly includes a continuous coding region for polypeptide SEQ ID NO:9. Differently, the nucleic acid disclosed in Lin includes a predicted gene, in which the coding region for SEQ ID NO:9 is interrupted by **four intron sequences**. Since the claimed nucleic acid does not include these **intron sequences**, it clearly is different from the nucleic acid disclosed in Lin. In other words, Lin does not anticipate claim 1 as amended. Nor does it anticipate claims 8 and 30-33, which depend, directly or indirectly, from claim 6.

Turning to claim 7, this claim covers an isolated nucleic acid that, under a high stringency condition, hybridizes to a probe containing the sequence of SEQ ID NO:20. As stated above, Lin teaches a nucleic acid including a predicted gene that encodes SEQ ID NO:9. This predicted gene includes five exons separated by four introns, which are not present in SEQ ID NO:20. Given the existence of the four introns, the predicted gene, as a whole, has low homology to SEQ ID NO:20. Therefore, a skilled artisan would readily recognize that it does not hybridize to a probe containing the sequence of SEQ ID NO:20 under a high stringency condition, a limitation recited in claim 7. Of note, this predicted gene (1834 bp) constitutes only one fifth of the nucleic acid disclosed in Lin (86022 bp). In other words, 80% of the nucleotide sequence of this nucleic acid has no homology at all to SEQ ID NO:20. A fortiori, one of ordinary skill in the art would have no doubt that the whole nucleic acid disclosed in Lin cannot hybridize to SEQ ID NO:20 under a high stringency condition. In other words, Lin also does not anticipate claim 7, as well as its dependent claim 9.

Rejections under 35 USC § 103

Claims 6-15 and 30-33 stand rejected as being obvious over Lin and in view of Maniatis et al. ("Maniatis").[1] Applicants disagree.

Claims 6-13 and 30-33 each cover a nucleic acid containing a cDNA sequence that encodes a polypeptide which is at least 70% identical to SEQ ID NO:9, or hybridizes to SEQ ID NO:20 (encoding SEQ ID NO:9), as well as a vector or a host cell containing the nucleic acid. Lin discloses the genomic sequence of Arabidopsis thaliana chromosome III and predicts open reading frames located therein, one of which matches SEQ ID NO:20. At issue here is whether a genomic sequence containing a predicted open reading frame would render obvious a cDNA sequence that matches the predicted open reading frame.

It is well known in the art that (1) a cDNA sequence corresponds to a functional gene, a gene that encodes a protein and is expressed in an organism, and that (2) a genomic sequence represents the raw nucleotide sequence of a genome, or a portion thereof. While open reading frames (ORF) are routinely predicted based on genomic sequences, there is no certainty that all of the predicted ORFs are actually functional genes. More specifically, most genomes contain pseudogenes that are structurally similar to functional genes and would be predicted as open reading frames. Of note, they do not encode proteins and are not expressed in an organism. Because of their structural similarity, it is difficult to one of ordinary skill in the art to determine whether a genomic sequence contains an actually functional gene or just a pseudogene. For this very reason, the number of human functional genes is still unclear even though the human genome was completely sequenced as early as 2003.

Taken together, it would not be obvious to one skilled in the art to recognize all functional genes based on a genomic sequence containing these genes. Accordingly, an artisan also would not readily recognize a cDNA sequence, which corresponds to a functional gene, based on a genomic sequence. In other words, Lin does not render claims 6-13 and 30-33 obvious.

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[1] In view of the Office Action, Applicants believe that the Examiner rejects claims 6-13 and 30-33 as being obvious over Lin and rejects claims 14 and 15 as being obvious over Lin in view of Maniatis. Applicants address below the rejection accordingly.

Claims 14 and 15, which depend indirectly from claims 6 and 7, respectively, are drawn to a method of producing a polypeptide by expressing the claimed nucleic acids in a cell. As discussed above, Lin does not render the claimed nucleic acid obvious. While teaching a method of expressing a nucleic acid sequence of interest in a cell, Maniatis does not teach or suggest the claimed nucleic acid. Therefore, the combined teachings of the two references does not render the claimed methods obvious.

Rejections under 35 USC § 112, Second Paragraph

Claims 7, 9, 11, 13, 15, 27, and 29 are rejected as being indefinite. Applicants have amended independent claim 7, reciting "a probe comprising the sequence of SEQ ID NO:20," following the Examiner's instructions. This amendment is believed to have overcome the rejection of claim 7, as well as the other claims which depend from claim 7.

Rejections under 35 USC § 112, First Paragraph (Enablement)

The Examiner rejects claims 6-15 and 30-33 for lack of enablement. According to the Examiner, "the specification, while being enabling for an isolated nucleic acid comprising a sequence that encode the polypeptide of SEQ ID NO:9, does not reasonably provide enablement for a nucleic acid that encodes for a polypeptide which has less than 100% sequence identity to SEQ ID NO:9." See the Office Action, page 2, section 4. Applicants respectfully traverse.

Apparently referring to claim 6, the Examiner asserts that a polypeptide with 70% identity to SEQ ID NO:9 would most likely lose its activity in view of Guo. Claim 6 covers a nucleic acid containing a sequence that encodes a polypeptide at least 70% identical to SEQ ID NO:9 and retains its activity, i.e., increasing sensitivity of a plant to an environmental factor. Guo teaches that 34% of **random** amino acid replacements in a protein would lead to inactivation of the protein. Based on this teaching, it is the Examiner's position that the probability factor of protein inactivation would reach 1020% (34x30) when making a polypeptide that is 70% identical to a known protein. See the Office Action, page 4, first paragraph.

Applicants disagree. First, one of ordinary skill in the art would not apply random amino acid replacements for making the polypeptide recited in claim 6, i.e., at least 70% identical to SEQ ID NO:9 and retains its activity. In fact, one skilled in the art would know what types of mutations to make and where to insert them in SEQ ID NO:9 so that the resulting polypeptide would retain the activity. For example, a skilled artisan would make conservative amino acid substitutions since they would not cause any dramatic impact on the function of a protein. Further, the present specification identifies domains of AtTLP9 (SEQ ID NO:9) that are conserved in the AtTLP family, i.e., tubby domain, F-box, TUB1 and TUB2 motifs. See page 17, lines 16-31, and page 18, lines 1-11. One skilled in the art would know to avoid those conserved domains or make only conservative changes so that the resulting polypeptides would more likely retain the activity of SEQ ID NO:9. Applying these approaches, a polypeptide so made having 70% identity to SEQ ID NO:9 would have a much lower probability of losing its activity, compared to that of the polypeptides made by introducing random amino acid replacements as taught in Guo.

Second, the Examiner asserts that even a polypeptide having at least 95% identity to a known protein would be unlikely to preserve the function because the probability factor of protein inactivation would be 170% (34% x 5) in this case according to Guo. It appears to be the Examiner's position that the present specification does not enable even a polypeptide that is at least 95% identical to SEQ ID NO:9.[2]

Applicants would like to bring to the Examiner's attention the Example 14 of the "Written Description Guidelines" ("Guideline"). In this example, the claim is directed to a "protein having SEQ ID NO:3 and variants thereof that are at least 95% identical to SEQ ID NO:3 and catalyze the reaction of A→ B." The Guideline concludes that this claim meets the written description requirement but is silent as to whether it also meets the enablement requirement. Applying the Examiner's logic iterated above, this claim would fail to satisfy the enablement requirement. However, Applicants cannot envision that the Office would provide an example that meets one requirement but not another since doing so would render the example meaningless and even misleading. In view of these considerations, Applicant submit that it is inappropriate to apply the

[2] Indeed, the Examiner rejects claim 32, which covers a nucleic acid encoding a polypeptide at least 95% identical to SEQ ID NO:9.

probability factor taught in Guo in the present application to predict that a polypeptide less than 100% identical to SEQ ID NO:9 would most likely lose the specified activity.

It is true that polypeptides having at least 70% identity to SEQ ID NO:9 would inevitably include those which lose the activity of SEQ ID NO:9, regardless of which approach is adopted in making them. This fact, however, does not compel the conclusion that undue experimentation would be needed to practice claim 6. Indeed, the polypeptides covered by claim 6 are limited to those having the activity of increasing sensitivity of a plant to an environmental factor. In other words, it does not encompass polypeptides that are at least 70% identical to SEQ ID NO:9 but lose its activity. In addition, the specification adequately teaches assays for testing mutants of SEQ ID NO:9 to screen for those retaining the specified activity as required by claim 6. See pages 22-25. In view of these teachings, Applicants submit that only routine experimentation would be needed to a skilled in the art to make and use the claimed nucleic acid, i.e., making a nucleic acid encoding a polypeptide at least 70% identical to SEQ ID NO:9, and then screening for those that retain the activity using the assays taught in the specification.

In view of the above remarks, claim 6 clearly meets the enablement requirement. So do claims 8, 10, 12, 14, and 30-33, which depend from claim 6, directly or indirectly.

Claim 7, the other independent claim, covers a nucleic acid that hybridizes to SEQ ID NO:20 under a high stringency condition and encodes a polypeptide that has activity of increasing the sensitivity of a plant to an environmental factor. The Examiner alleges that it "would encompass the hybridization of a nucleic acid sequence unrelated to SEQ ID NO:20, which may not have the activity of increasing the sensitivity of a plant to an environmental factor;" and that "undue experimentation is required by skilled artisan to determine how to use said unrelated nucleic acid sequences that hybridize to SEQ ID NO:9 (should read "SEQ ID NO:20") in a method of increasing sensitivity of a plant to an environmental factor." See the Office Action, pages 4-5.

It appears that the Examiner has overlooked the limitation "encodes a polypeptide that has activity of increasing the sensitivity of a plant to an environmental factor," recited in claim 7. Clearly, claim 7 covers nucleic acids that hybridize to SEQ ID NO:20 and retain the recited function. Accordingly, the Examiner's above allegation is fallacious.

As stated above, the specification teaches how to determine whether a polypeptide retains the specified activity. See pages 22-25. Thus, only routine experimentation would be needed for a skilled in the art to make and use the claimed nucleic acid, i.e., making a nucleic acid that hybridizes to SEQ ID NO:20 and then selecting those that encode a polypeptide retaining the activity.

Accordingly, claim 7, as well as its dependent claims 9, 11, 13, and 15, meets the enablement requirement.

Rejection under 35 USC § 112, First Paragraph (Written Description)

The Examiner maintains the rejections of claims 6-14 and further rejects claims 15 and 26-33 for lack of written description on various grounds.

First, the Examiner rejects Applicants' argument that claim 7 is analogous to Example 9 of the Guideline on the ground that Example 9 provides a working example of using a DNA to isolate nucleic acids that hybridize to it under a high stringency condition, while the present specification does not. See the Office Action, page 6, first paragraph.

Applicants disagree. Claim 7 and the claim in Example 9 are very similar: both cover a genus of nucleic acids that hybridize to a defined sequence under a high stringency condition and encode a polypeptide having a particular function. The Analysis of Example 9 ("Analysis") states"

> There is a single species disclosed (a molecule consisting of SEQ ID NO:1 (the defined sequence) that is within the scope of the claimed genus. There is actual reduction of practice of the disclosed species. Now turning to the genus analysis, a person of skill in the art would not expect substantial variation among species encompassed within the scope of the claims because the highly stringent hybridization conditions set forth in the claim yield structurally similar DNAs. Thus, a representative number of species is disclosed, since highly stringent hybridization conditions in combination with the coding function of DNA and the level of skill and knowledge in the art are adequate to determine that applicant was in possession of the claimed invention.

Based on this analysis, it is concluded that the claimed nucleic acid in Example 9 is adequately described.

In view of Example 9 and the present specification, Applicants submit that all arguments presented in the Analysis would lead to the conclusion that claim 7 satisfies the written description requirement. The specification disclose a species, SEQ ID NO:20, which falls into the claimed genus. No doubt that this species has been reduced to practice. Further, the term "under a high stringency condition" recited in claim 7 is defined as "hybridization at 65°C, 0.5 X SSC, followed by washing at 45°C, 0.1 X SSC." One skilled in the art would understand that such a high stringency would only yield DNAs that are structurally similar to SEQ ID NO:20. In addition, the claimed nucleic acids are limited to those that encode polypeptides having activity of increasing the sensitivity of a plant to an environmental factor. In view of the high stringency condition and the coding function of the claimed nucleic acid, one skilled in the art would readily conclude that Applicants were in possession of the claimed nucleic acid at the time when this application was filed.

The Examiner relies on the working example taught in Example 9 to distinguish it from claim 7. Applicants note that this working example is not even mentioned in the Analysis that leads to the conclusion that the claim in Example 9 meets the written description requirement.[3] In other words, lack of such a working example would not render inadequately described the claimed nucleic acid in Example 9. By the same token, it follows that claim 7 does not fail to meet the written description requirement.

In view of the above discussion, Applicants submit that claim 7, as well as its dependent claims 9, 11, 13, 15, 27, and 29, meets the written description requirement.

Next, the Examiner disagrees that claim 6 is highly analogous to the claim in Example 14 of the Guideline, alleging that claim 6 recites 70% sequence identity to a defined sequence, which is a much broader genus than that covered by the claim in Example 14, reciting 95% sequence identity to a defined sequence.

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[3] In this working example, several nucleic acids were isolated, expressed and some of them were shown to encode proteins having the specified function. However, these hybridizing nucleic acids were not sequenced. Therefore, this working example does not teach how structurally similar these nucleic acids were compared to SEQ ID NO:1. Accordingly, this working example does not support the statement in the Analysis that "the highly stringent hybridization conditions set forth in the claim yield structurally similar DNAs." In other words, this statement can be based only on knowledge in the pertinent art.

Applicants respectfully disagree. Although the claim in Example 14 recites 95% sequence identity to a defined sequence, nowhere in this example or in the MPEP states that a claim reciting any sequence identity lower than 95% would for sure fail to meet the written description requirement. In other words, the Office has not set forth 95% sequence identity or higher as the written description standard for claims directed to protein variants.

As mentioned above, claim 6 covers a nucleic acid encoding a polypeptide that is at least 70% identical to SEQ ID NO:9 and has the activity of increasing the sensitivity of a plant to an environmental factor. The specification discloses the full amino acid sequence of AtTLP9 (SEQ ID NO:9) and the cDNA sequence that encodes the protein (SEQ ID NO:20). It further teaches that most members of the AtTLP family, including AtTLP9 (SEQ ID NO:9), have a well-conserved tubby domain at their C-terminus, a conserved F-box containing domain, and two TUB motifs (TUB1 and TUB2). Based on these teachings, one skilled in the art could infer the whole structure of the polypeptide encoded by the claimed nucleic acid. In other words, a skilled artisan would readily recognize that Applicants were in possession of the polypeptide recited in claim 6 at the time this application was filed. Since the genetic code is well known, one skilled in the art would also conclude that Applicants were in possession of the claimed nucleic acid, which encodes that polypeptide. Accordingly, claim 6 meets the written description requirement. So do claims 8, 10, 12, 14, 26, 28 and 30-33, all dependent from claim 6, directly or indirectly.

CONCLUSION

In view of the above remarks, Applicants submit that grounds for rejections asserted by the Examiner have been overcome. The claims, as amended, are not anticipated, or rendered obvious by Lin, and meet the written description and enablement requirements. On this basis, it is submitted that allowance of this application is proper, and early favorable action is respectfully solicited.

Enclosed is a $60 check for the Petition for Extension of Time fee. Please apply any other charges or credits to deposit account 06-1050.

Respectfully submitted,

Date: 11/28/2006

Y. Jenny Chen, Ph.D., J.D.
Attorney for Applicants
Reg. No. 55,055

Fish & Richardson P.C.
225 Franklin Street
Boston, MA 02110
Telephone: (617) 542-5070
Facsimile: (617) 542-8906

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